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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,775	06/30/2006	Georg Feger	ARS-117	1797

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EXAMINER	
MACFARLANE, STACEY NEE	
ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,775	FEGER ET AL.	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-31,33-39 and 44-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-31, 33-39, 44-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/18/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims26, 33, 34, 39 have been amended, claims 40-43 cancelled and claims 44-61 are newly added as requested in the amendment filed on June 2, 2008. Following the amendment, claims 26-31, 33-39 and 44-61 are pending in the instant application.

Claims 28-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions, there being no allowable generic or linking claim.

Claims 26, 27, 33-39 and 44-61 are under examination in the instant office action.

2. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

3. Applicant's arguments filed on June 2, 2008 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 26, 27, 33-39 and 44-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 26 is vague and indefinite in so far as it employs the term "clusterin fusion protein" as a limitation and while the clusterin is defined with a reference to a precise amino acid sequence identified by a proper SEQ ID NO:, one of ordinary skill in the art cannot determine the metes and bounds of the fusion protein because the components are not clearly defined. Moreover, because the instant specification does not identify that property or combination of properties which is unique to and, therefore, definitive of a clusterin fusion protein, an artisan cannot determine if a compound would be included or excluded from the claimed subject matter by the presence of this limitation.

7. Claims 27, 33-39 and 44-61 are included in the rejection because they depend from an indefinite claim.

New Grounds – Necessitated by Amendment

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. As currently amended, Claims 26, 27, 26, 27, 33-39 and 44-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating the instantly-elected condition of traumatic nerve injury comprising the administration of a full-length clusterin polypeptide comprising SEQ ID NO:1, does not reasonably provide enablement for any other condition besides peripheral traumatic nerve injury. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

As currently amended, Claim 26 broadly encompasses a method of treating *any* peripheral neurological disease comprising administering a clusterin polypeptide comprising SEQ ID NO: 1, or a peptide comprising amino acids 23-449, 35-449, 23-227, 35-227 or 228-449 of SEQ ID NO: 1 thereof.

With respect to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the scope of enablement, the claims are analyzed with respect to the teachings of the specification and are to be given their broadest reasonable interpretation that is consistent with the specification. See MPEP 2111 [R-1], which states: "During patent examination, the pending claims must be "given *>their< broadest reasonable interpretation consistent with the specification." In re Hyatt, 211 F.3d 1367, 1372, 54 USPQ2d 1664, 1667 (Fed. Cir. 2000). Applicant always has the opportunity to amend the claims during prosecution, and broad interpretation by the examiner reduces the possibility that the claim, once issued, will be

interpreted more broadly than is justified. In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550- 51 (CCPA 1969)".

As such, the broadest reasonable interpretation of the claimed method is that it allows the treatment of *any* peripheral neurological disease. Thus, the claims encompass an unreasonable number of pathologically distinct conditions and disorders, including genetically inherited diseases, such as Charcot-Marie-Tooth disease. The etiological, pathological and symptom profiles of many of these encompassed diseases and conditions have no nexus to or association with clusterin polypeptide. Thus, a skilled artisan would not know how to treat these diseases based solely on the administration of a clusterin polypeptide.

As opposed to the claims, what is disclosed about the claimed method is narrow: The working examples provide guidance as to the intraperitoneal or subcutaneous administration of *full-length* recombinant clusterin as alleviating the pathological manifestations of peripheral nerve crush damage, as assessed by electrophysiological measurements and morphometric analysis. Thus, the specification provides guidance for the treatment of peripheral traumatic nerve injury via a mouse model. The specification, however, provides no direction or guidance as to how one of ordinary skill in the art would practice the method with a reasonable expectation of success for the treatment of *any other* peripheral neurological disease. Therefore, the disclosure provides no guidance as to how to use the invention to the full extent of the scope claimed.

The invention is based on the findings that treatment with mature recombinant clusterin has the following results within a mouse model for traumatic nerve injury: (1) significant increase in the compound muscular action potential and a decrease in latency of the potential as compared to untreated controls (pages 35-36). Morphometric analysis demonstrated a significantly decreased proportion of degenerated fibers as compared to untreated controls.

However, the instant specification provides neither enough guidance nor evidence in the form of working examples, which would show that the claimed method was successfully achieved for the treatment of any other peripheral neurological disease. Absent such guidance, one of ordinary skill in the art would need to look to the state of the art at the time of filing to discover how to practice Applicant's invention, as currently claimed.

It had long been known in the art, prior to filing that clusterin mRNA and protein are upregulated following peripheral nerve injury (Liu et al. Neuroscience 68(1): 167-179, 1995) and that its role in neural degeneration and regeneration could provide new insights into new therapeutic approaches for nerve injury (Törnqvist et al., Neurobiology of Aging, 17(5):696-705, 1996), but these findings had not been expanded to application of the method with respect to any peripheral nerve disease. In the prostate, overexpression of clusterin or clusterin agonists had been demonstrated to decrease cell cycle progression (Betuzzi et al., Oncogene, 21:4328-4334, 2002). But the effects of recombinant full-length clusterin protein in vivo had not been explored at all and no nexus between clusterin polypeptide and peripheral diseases in general had been

provided within the art. Absent such teachings within the art and barring guidance within the instant specification, one of ordinary skill in the art would have had to perform undue experimentation in order to practice the method to the full scope of the claims.

The standard of an enabling disclosure is not the ability to make and test if the invention works but one of the ability to make and use with a reasonable expectation of success. A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of Genentech, Inc, v. Novo Nordisk, 42 USPQ 2d 1001, (CAFC 1997), the court held that:

> "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution in order to use the invention comprising a clusterin polypeptide, and then demonstrate that the clusterin polypeptide are effective to treat a vast array of pathologically distinct peripheral neurological diseases. Therefore, Claims 26, 27, 33-39 and 44-61 are rejected under 35 U.S.C. 112, first paragraph, for failing to meet the enablement requirement commensurate in scope with these claims.

Conclusion

10. No Claim is allowed.

11. This application contains claims drawn to an invention nonelected without traverse in Paper filed on November 19, 2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M,W and ALT F 7 am to 3:30, T & R 5:30 -5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/Olga N. Chernyshev, Ph.D./
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